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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,079	10/02/2003	Iris Pecker	26871	7751

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EXAMINER	
DIBRINO, MARIANNE NMN	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/676,079	PECKER ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-15 and 23-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-15 and 23-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 1/17/06 is acknowledged and has been entered.

It is noted that there is an inconsistency in the subject line on the first page of Applicant's amendment, *i.e,* "For: Assessing the Color of Finished Diamonds from a Rough Diamond" refers to a different title than the title of the instant application.

2. Applicant is reminded of Applicant's election of SEQ ID NO: 1 as the species of polynucleotide sequence, SEQ ID NO: 6 and 7 as the species of pair of oligonucleotides comprising a sense oligonucleotide and an antisense oligonucleotide, and light emitting moiety as a species of specific detectable moiety in Applicant's response filed 10/29/04.

Claims 4-15 and newly added claims 23-28 read on the elected species and are currently being examined.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 10-15 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not disclosed in the specification and claims as originally filed is "a kit."

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 4-15 and 23-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 10 are indefinite in the recitation of "being capable of directing" because it is not clear what is meant. It is suggested that Applicant amend said claims to recite "said pair of oligonucleotides capable of directing...."

7. For the purpose of prior art rejections, the filing date of the instant claims 10-15 and 26-28 is deemed to be the filing date of the instant application, *i.e.* 10/2/03, as the parent applications do not support the claimed limitation "kit."

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 10-12 and 26-28 are rejected under 35 U.S.C. 102(b) as being anticipated by US 2002/0102560 A1 (of record).

US 2002/0102560 A1 discloses the PCR primers HPU-355 and HPL-229 that are SEQ ID NO: 6 and 7, respectively of the instant application (especially pages 17-18). US 2002/0102560 A1 further teaches labeling heparanase hybridizing polynucleotide probes with fluorescent tags for *in situ* detection in chromosome spreads (especially page 15 and claims). US 2002/0102560 A1 discloses expression of heparanase by cells of the immune system, and use of heparanase specific probes for immunodetection and diagnosis of micrometastases in biopsy specimens, *i.e., in situ* (especially page 15). US 2002/0102560 A1 further discloses use of a kit for PCR amplification of heparanase cDNA, said kit comprising heparanase specific sense and anti-sense primers that were used to amplify a portion of human heparanase oligonucleotide sequence SEQ ID NO: 9 (SEQ ID NO: 1 of the instant claims) that encodes SEQ ID NO: 10 (SEQ ID NO: 2 of the instant claims) or a variant with phenylalanine at position 246 instead of tyrosine, *i.e.,* Y246F, that is produced by an A799T substitution in SEQ ID NO: 9 (SEQ ID NO: 1 of the instant claims) (especially [0263]-[0264], Figure 1, [0243], abstract). US 2002/0102560 A1 discloses using PCR to demonstrate expression of heparanase gene in human tissues and cells (especially [0143]).

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 10 and 13-15 are rejected under 35 U.S.C. 103(a) as being obvious over US 2002/0102560 A1 (of record) in view of RT-PCR Methods & Applications Book 1 (of record).

US 2002/0102560 A1 discloses the PCR primers HPU-355 and HPL-229 that are SEQ ID NO: 6 and 7, respectively of the instant application (especially pages 17-18). US 2002/0102560 A1 further teaches labeling heparanase hybridizing polynucleotide probes with fluorescent tags for *in situ* detection in chromosome spreads (especially page 15 and claims). US 2002/0102560 A1 discloses expression of heparanase by cells of the immune system, and use of heparanase specific probes for immunodetection and diagnosis of micrometastases in biopsy specimens, *i.e., in situ* (especially page 15). US 2002/0102560 A1 further discloses use of a kit for PCR amplification of heparanase cDNA, said kit comprising heparanase specific sense and anti-sense primers that were used to amplify a portion of human heparanase oligonucleotide sequence SEQ ID NO: 9 (SEQ ID NO: 1 of the instant claims) that encodes SEQ ID NO: 10 (SEQ ID NO: 2 of the instant claims) or a variant with phenylalanine at position 246 instead of tyrosine, *i.e.,* Y246F, that is produced by an A799T substitution in SEQ ID NO: 9 (SEQ ID NO: 1 of the instant claims) (especially [0263]-[0264], Figure 1, [0243], abstract). US 2002/0102560 A1 discloses using PCR to demonstrate expression of heparanase gene in human tissues and cells (especially [0143]).

US 2002/0102560 A1 does not disclose wherein either the sense or antisense oligonucleotide is labeled with a detectable moiety, including those recited in instant claims 14 and 15, nor wherein the PCR primer oligonucleotides HPU-355 and HPL-229 that are SEQ ID NO: 6 and 7, respectively, of the instant application are included in a kit.

RT-PCR Methods & Applications Book 1 teaches primer design and labeling of one or both PCT primers with radioactive detectable moiety γ^{32} P-ATP for quantitation of PCR-amplified products (especially pages 26 and 40).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have labeled SEQ ID NO: 6 and 7 taught by US 2002/0102560 A1 with the fluorescent tag taught by of US 2002/0102560 A1 or with the radioactive moiety taught by RT-PCR Methods & Applications Book 1, and to have included the oligonucleotide PCR primers (SEQ ID NO: 6 and 7) in a kit as disclosed by US 2002/0102560 A1 for other components of the PCR amplification procedure.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to perform *in situ* hybridization for detecting the presence of heparanase in biopsy specimens as disclosed by US 2002/0102560 A1 and because RT-PCR Methods & Applications Book 1 also teaches labeling of one or more of the PCR primers for quantitation of PCR-amplified products, and US 2002/0102560 A1 discloses the use of kits for PCR amplification and one of ordinary skill in the art would have recognized the convenience of using the kit for immunodetection and diagnosis of heparanase as disclosed by US 2002/0102560 A1.

12. Claims 10-15 and 26-28 are rejected under 35 U.S.C. 103(a) as being obvious over WO 99/11798 A1 (of record) in view of RT-PCR Methods & Applications Book 1 (of record), pET System Manual 6th Edition (of record) and Ennis et al (PNAS USA 87: 2833-2837, 1990, of record).

WO 99/11798 A1 teaches the PCR primers HPU-355 and HPL-229 which are SEQ ID NO: 6 and 7, respectively of the instant application as well as of WO 99/11798 (especially page 23 at lines 23-34). WO 99/11798 A1 further teaches labeling heparanase hybridizing polynucleotide probes such as with fluorescent tags and use in *in situ* detection (especially page 20 and claims). WO 99/11798 A1 teaches expression of heparanase by cells of the immune system, and use of heparanase specific probes for immunodetection and diagnosis of micrometastases in biopsy specimens, *i.e., in situ* (especially pages 4-6 and 15). WO 99/11798 A1 teaches the primers amplify a portion of human heparanase oligonucleotide sequence SEQ ID NO: 9 (SEQ ID NO: 1 of the instant claims) that encodes SEQ ID NO: 10 (SEQ ID NO: 2 of the instant claims) or a variant with phenylalanine at position 246 instead of tyrosine, *i.e.,* Y246F, that is produced by an A799T substitution in SEQ ID NO: 9 (SEQ ID NO: 1 of the instant claims) (especially Examples, Figure 1 on page 1/14, sequence listing and abstract).

WO 99/11798 A1 does not teach wherein either the sense or antisense oligonucleotide is labeled with a detectable moiety, including those recited in instant claims 14 and 15, nor wherein at least one of the oligonucleotides is designed having an endonuclease cleavage site, nor wherein the said oligonucleotides are included in a kit.

RT-PCR Methods & Applications Book 1 teaches primer design and labeling of one or both PCT primers with radioactive detectable moiety γ^{32} P-ATP for quantitation of PCR-amplified products (especially pages 26 and 40).

Ennis *et al* teach PCR provides an approach to analyze target DNA sequences, and the use of a kit for PCR.

pET System Manual 6th Edition teaches using PCR to add restriction enzyme sites, *i.e.,* endonuclease cleavage sites, by adding the appropriate nucleotide sequences to the primer(s) for cloning of the PCR product (page 11).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have labeled SEQ ID NO: 6 and 7 taught by WO 99/11798 A1 with the fluorescent tag taught by WO 99/11798 A1 or with the radioactive moiety taught by RT-PCR Methods & Applications Book 1, to have added a restriction enzyme site as taught by pET System Manual 6th Edition, and to have included the sense and antisense oligonucleotide PCR primers (SEQ ID NO: 6 and 7) in a kit.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to perform in situ hybridization for detecting the presence of heparanase in biopsy specimens as taught by WO 99/11798 A1 and because RT-PCR Methods & Applications Book 1 also teaches labeling of one or both PCR primers for quantitation of PCR-amplified products, and pET System Manual 6th Edition teaches addition of restriction enzyme sites for cloning of PCR product. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to perform PCR amplification more conveniently for the applications taught by WO 99/11798 A1 since Ennis *et al* teach the advantage of using a kit for PCR amplification and WO 99/11798 A1 teaches expression of heparanase by cells of the immune system, and use of heparanase specific probes for immunodetection and diagnosis of micrometastases in biopsy specimens, *i.e., in situ.*

13. Claims 10-15 and 26-28 are rejected under 35 U.S.C. 103(a) as being obvious over WO 99/57153 A1 (of record) in view of RT-PCR Methods & Applications Book 1(of record), pET System Manual 6th Edition (of record), and Ennis *et al* (PNAS USA 87: 2833-2837, 1990, of record).

WO 99/57153 A1 teaches the PCR primers HPU-355 and HPL-229 that are SEQ ID NO: 6 and 7, respectively of the instant application (especially pages 29-30 at the spanning paragraph). WO 99/57153 A1 teaches *in situ* hybridization with two digoxigenin (a chromogenic label) probes for detection of heparanase transcripts in normal and malignant tissues by PCR amplification (especially page 30, legends for Figures 3-5, 7-15). WO 99/57153 A1 teaches a pair of polymerase chain reaction primer sense and antisense oligonucleotides and use in PCR and detection of heparanase (especially page 23 and claims 17, 18 and 32). WO 99/57153 A1 teaches the ingredients needed for PCR include reagents for extracting mRNA from a biological sample, reagents for reverse transcribing mRNA into cDNA, a pair of heparanase specific PCR primers, nucleoside triphosphates and a thermostable DNA polymerase (especially last two paragraphs on page 23). WO 99/57153 A1 teaches a detectable moiety can be used to label a synthetic oligonucleotide of the invention, and that the detectable moiety can be radioactive isotopes, enzymes that can catalyze color or light emitting reactions and fluorophores (especially paragraph spanning pages 21 and 22). SEQ ID NO: 1 is heparanase cDNA and SEQ ID NO: 2 is heparanase protein (sequence listing).

WO 99/57153 A1 does not teach wherein wherein at least one of the oligonucleotides is designed having an endonuclease cleavage site, nor wherein the primers are included in a kit.

RT-PCR Methods & Applications Book 1 teaches primer design and labeling of one or both PCT primers with radioactive detectable moiety gamma-32 P-ATP for quantitation of PCR-amplified products (especially pages 26 and 40).

pET System Manual 6th Edition teaches using PCR to add restriction enzyme sites by adding the appropriate nucleotide sequences to the primer(s) for cloning of the PCR product (page 11).

Ennis *et al* teach PCR provides an approach to analyze target DNA sequences, and the use of a kit for PCR.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have labeled SEQ ID NO: 6 and 7 taught by WO 99/57153 A1 with the fluorescent tag or any detectable moiety taught by WO 99/57153 A1 or with the radioactive moiety taught by RT-PCR Methods & Applications Book 1, to have added an endonuclease cleavage site as taught by pET System Manual 6th Edition, and to have included the oligonucleotide sense and antisense primers (SEQ ID NO: 6 and 7) for PCR in a kit as taught by Ennis *et al* for other components of PCR.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to perform *in situ* hybridization for detecting the presence of heparanase in biopsy specimens as taught by WO 99/57153 A1 and because RT-PCR Methods & Applications Book 1 also teaches labeling of one or more of the PCR primers for quantitation of PCR-amplified products, pET System Manual 6th Edition teaches adding restriction enzyme sites to a primer(s) for cloning of the PCR product, and Ennis et al teach the advantage of using a kit for PCR in order to analyze target DNA sequences. One of ordinary skill in the art would at the time the invention was made would have been motivated to do this because WO 99/57153 A1 teaches *in situ* hybridization for detection of heparanase transcripts in normal and malignant tissues by PCR amplification as well as the ingredients needed for PCR, and one of skill in the art would have recognized that the convenience of using a kit taught by Ennis *et al* would be enhanced for applications such as taught by WO 99/57153 A1.

With respect to the recitation of SEQ ID NO: 1 or the A799T variant or SEQ ID NO: 2 or the Y246F variant, it is an expected property that SEQ ID NO: 6 and 7 are capable of directing PCR amplification resulting in a polynucleotide fragment of SEQ ID NO:1 that encodes SEQ ID NO:2, or resulting in a polynucleotide fragment of the A799T variant that encodes the Y246F variant.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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